Clinicopathological and immunohistochemistry correlation in a case of Vogt-Koyanagi-Harada disease

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Vogt-Koyanagi-Harada (VKH) disease is a systemic disorder causing bilateral panuveitis. Histopathological documentation along with molecular diagnostic evidence in VKH eye is a rarity. We present a 46-year-old woman with VKH with several ocular complications and subsequently enucleation of the right eye was done because of painful blind eye. Patient had clinical complications of VKH and some of the complications were observed in histopathology. Pathology of the case showed nongranulomatous uveitis, indicating the disease in chronic recurrent stage. Immunohistochemistry showed predominant T-cell involvement in this case. The case showed clinicopathological and immunohistochemistry correlation in a case of VKH disease.

Key words: Choroid, choroidal neovascular membrane, immunohistochemistry, panuveitis, Vogt-Koyanagi-Harada disease

Vogt-Koyanagi-Harada (VKH) disease is a multisystem disorder which includes panuveitis of both the eyes with meninges, ears, and skin involvement.[1-10] Criteria of VKH was devised and revised time to time.[1-4] Clinical course of VKH is varied.[1-5] There are four stages of VKH, namely, prodromal, uveitic, chronic, and chronic recurrent stage.[1-4] Pathology of VKH and its similar disease condition sympathetetic ophthalmia (SO) are very interactive.[4] Compared with SO, VKH eyeball specimens are rarely available.[4] We present a rare case of VKH in a 46-year-old Indian woman presented with bilateral panuveitis. During the course of the disease, one of the eyes had been enucleated for painful blind eye and was documented histopathologically (HPE) and by immunohistochemistry (IHC).

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1800_18

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Manuscript received: 29.10.18; Revision accepted: 15.02.19

Case Report

A 46-yr-old woman came to outpatient department at our referral center in South India with chief complains of pain in both eyes (OU) and dimness of vision since 10 months. She was seen elsewhere and was diagnosed as a case of VKH. She was investigated thoroughly and other causes of panuveitis were ruled out. Her best corrected visual activity was light perception with inaccurate projection of rays in the right eye (OD) and 6/15 in the left eye (OS). Her intraocular pressure was unrecordable in OD and 17 mmHg in OS. On slitlamp examination, OD had corneal edema with Descemets folds, shallow anterior chamber with iris bombe, posterior synechiae, peripheral anterior synechiae, patent peripheral iridectomy, and complicated cataract with festooned pupil. Gonioscopy showed 360° peripheral anterior synechiae with iris root closed. OS had clear cornea with anterior chamber cells++, flare++, patent peripheral iridectomy, posterior synechiae with posterior subcapsular cataract. Fundus examination had no view in OD, OS had lens haze with attached retina. A diagnosis of hypotonous eye secondary to chronic uveitis complicated cataract with seclusio papillae was made. She was put on tablet azathioprine 50 mg three times daily with oral predinisdone 40 mg/day. Patient was advised to undergo cataract surgery (extracapsular cataract extraction with intraocular lens implantation with iris hooks under steroid cover) in OS. Cataract surgery was done 6 months later. Postoperatively she was found to have sunset glow fundus. A diagnosis of VKH was confirmed. There was no systemic feature. A diagnosis of incomplete VKH was made according to revised diagnostic criteria of VKH. She was lost to follow-up. She came back after 1 year with dimness of vision left eye. Her best corrected visual acuity was 6/60 in OS. Slit lamp examination of OD status quo and OS showed anterior chamber flare1, + cells1, + vitreous cells1 + posterior chamber intraocular lens *in situ*. Fundus examination showed depigmented fundus with sunset glow in the OS with choroidal neovascular membrane (CNVM). Optical coherence tomography (OCT) in OS showed choroidal neovascular membrane with cystoid macular edema. Three intravitreal avastin injections were given and finally CNVM regressed after third injection. At final visit, OS had depigmented fundus with sunset glow, with scarred CNVM. A diagnosis of VKH disease was made and patient was on azathioprine oral prednisolone 10 mg/day and prednisolone eye drops. Patient had a regular follow-up every 2 months and oral prednisolone was tapered. At 6 months follow-up visit, her best corrected visual acuity was 6/18 in the OS. Oral steroid was continued 10 mg/day along with topical prednisolone eye drops 3 times a day. Fundus showed depigmentation with sunset glow. Best corrected visual acuity in OS was 6/12. Right eye was painful blind with phthisis bulbi. She was advised for enucleation of OD after obtaining the informed consent.

Cite this article as: Das D, Boddepalli A, Biswas J. Clinicopathological and immunohistochemistry correlation in a case of Vogt-Koyanagi-Harada disease. Indian J Ophthalmol 2019;67:1217-9.

Enucleation done was after 1 month. Fundus examination in OS showed typical sunset glow suggestive of VKH disease.

The enucleated eyeball (OD) on histopathology showed anterior segment including lens in the section studied. Vitreous cavity showed red blood cells (RBC) with occasional lymphocytes. Posterior segment showed diffuse choroidal thickness with congested choroidal stromal vessels and full thickness inflammation by chronic inflammatory cells which included lymphocytes and plasma cells [Figs. 1 and 2]. There were reducing numbers of choroidal melanocytes. In retina, there were photoreceptor degenerations with multiple pockets of fluids in outer retinal layers. Bone formations were noted with focal retinal pigment epithelium (RPE) undulations. Areas of retinal gliosis were seen. Portion of the choroid under the degenerated RPE showed choroidal neovascularization with outpouring of RBCs. Sclera was thickened posteriorly. Immunohistochemistry showed CD3 (T-cell marker, CELL MARQUE, USA): +++, CD20 (B-cell marker, CELL MARQUE, USA): +[Figs. 3 and 4], slides were compared with controls. Significance of CD3 positivity indicated that T-cells involvements were predominant.

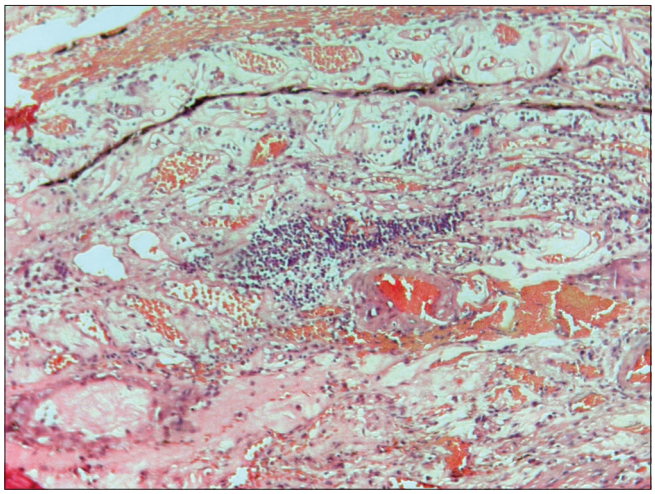

Figure 1: Light microscopy showed thickened, inflammed choroid in Hematoxylin eosin stained slide, 10×

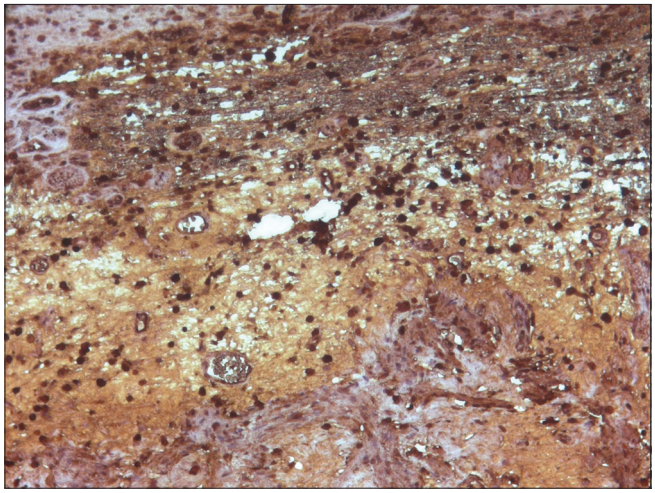

Figure 3: Immunostaining revealed CD3 (T cell Marker, CELL MARQUE, USA): +++, 20×

Discussion

VKH is a bilateral diffuse panuveitis with multisystem involvement.[1-10] In this case report, we highlighted in a middle-aged woman affected with bilateral panuveitis with other clinical ocular complications such as corneal edema, shallow anterior chamber, hypotonous right eye and cataract, sunset glow fundus, and CNVM in OS. Histopathology of the right eye showed congested choroidal stromal inflammation with marked thickening of retinochoraoidal complex. Inflammatory cells consisted of lymphocytes and plasma cells. The inflammation was nongranulomatous. It is important to note that in early stage of VKH, we may get nongranulomatous inflammation in the choroid also involving the choriocapillaries.[1-4] Presence of Dalen Fuch's-like nodules are seen mostly in chronic phase of VKH and not in the acute stage of the disease.[4] In chronic stage, there are RPE atrophic areas which can be picked up by indocyanine green angiography.[1-6] There were additional retinal changes in the histpathology in our case. Multiple fluid filled pockets were

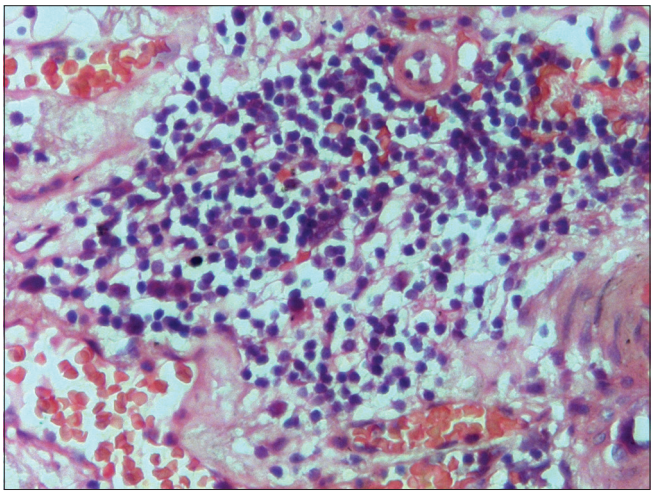

Figure 2: Light microscopy showed inflammatory cells infiltrate by plasma cells and lymphocytes in Hematoxylin and eosin stained slide, 40×

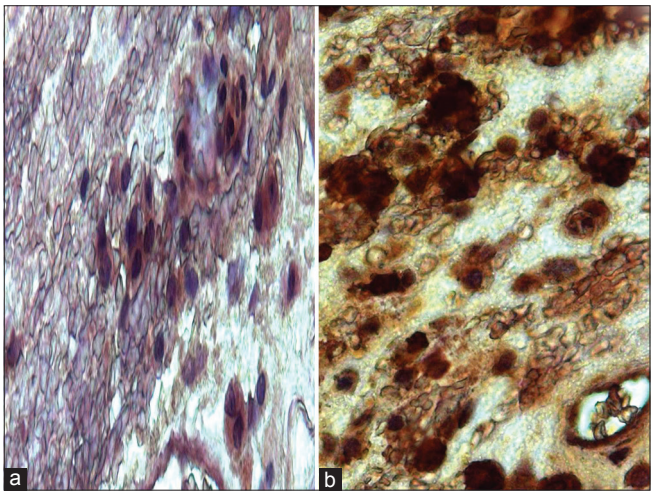

Figure 4: Showed comparative [a] CD 20+ (B-cell marker) and [b] CD 3+++ (T-cell marker) positivity (×40×)

seen in outer retinal layers with photoreceptors degenerations and retinal gliosis. Characteristically, the choroid showed reduced numbers of melanocytes which were the cause of depigmented fundus appearance. IHC showed predominance of T-cells expression which supported the pathogenesis of VKH being the T-cell-mediated disease.[4] Another characteristic HPE observation was that there was development of CNVM in the right eye also, which was seen even in the OS clinically and by OCT. The histopathological finding and immunohistochemistry were similar to sympathetic ophthalmia.

Conclusion

This interesting clinicopathological case of VKH with complications showed that it was in chronic recurrent stage supported by IHCs. The study also indicates that usage of early introduction of immunosuppressive and oral steroid is needed to prevent complications like recurrence of the disease with CNVM format.

Acknowledgements

Ms. K Vanitha, Technician ocular Pathology Department, Sankara Nethralaya Dept, and Mr Apurba Deka, M.Sc, Technician, Sri Sankaradeva Nethralaya Ocular Pathology Laboratory for IHC staining.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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